FORM PTO-1390 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NO. PHD 99,207
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. Application No. (if known, see 37 CFR 1.5) 10/069892
INTERNATIONAL APPLICATION NO. PCT/EP99/06348	INTERNATIONAL FILING DATE August 28, 1999	PRIORITY DATE CLAIMED August 28, 1999

TITLE OF INVENTION
AVOIDANCE OF POISONING EFFECTS DURING ANESTHESIA

APPLICANT(S) FOR DO/EO/US
Bernhard Fischer

Applicant(s) herewith submit to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.

2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.

3. [ ] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. [ ] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. [ ] copy of the International Application as filed (35 U.S.C. 371 (c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).

6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2))

7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.

8. [ ] A translation of the amendment to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).

9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.

12. [ ] An assignment document for recording. A separate cover sheet is compliance with 37 C.F.R. 3.28 and 3.31 is included.

13. [X] A FIRST preliminary amendment.
    [ ] A SECOND OR SUBSEQUENT preliminary amendment.

14. [ ] A substitute specification.

15. [X] A change of power of attorney and/or address letter.

16. [X] Other items or information:

    1 Sheets of Drawings

    X. Authorization Pursuant to 37 CFR § 1.136(a)(3) and to Charge Deposit Account

CERTIFICATE OF MAILING

[X] Express Mail Mailing Label No. EL 686950430 US
Date of Deposit 2-27-02
I hereby certify that this paper and fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Jeanne Rusciano
Typed Name

Jeanne Rusciano
Signature

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) 10/069892	INTERNATIONAL APPLICATION NO. PCT /EP99/06348	ATTORNEY'S DOCKET NUMBER PHD 99,207

17 [X] The following fees are submitted:

BASIC NATIONAL FEE (37 C.F.R. 1.492(A)(1)-(5)):

		CALCULATIONS (PTO USE ONLY)
Search Report has been prepared by the EPO or JPO	$860.00	
international preliminary-examination fee paid to USPTO (37 C.F.R. 1.482)	$690.00	
No international preliminary examination fee paid to USPTO (37 C.F.R. 1.482) but international search fee paid to USPTO (37 C.F.R. 1.445(a)(2)	$750.00	
Neither international preliminary examination fee (37 C.F.R. 1.482) nor international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO	$970.00	
international preliminary examination fee paid to USPTO (37 C.F.R. 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)	$ 96.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =		$ 860.00

Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 C.F.R. 1.492(e)).				$	
CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE	
Total Claims	8 - 20 =			X $ 18.00	$
Independent claims	4 - 3 =		1	X $ 84.00	$ 84.00
MULTIPLE DEPENDENT CLAIMS (if applicable)				+ $280.00	$
TOTAL OF ABOVE CALCULATIONS =					$ 84.00
Reductions by 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 C.F.R. 1.9, 1.27, 1.28)					$
SUBTOTAL =					$ 944.00
Processing fee of $130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 C.F.R. 1.492(f)). +					$
TOTAL NATIONAL FEE =					$ 944.00
Fee for recording the enclosed assignment (37 C.F.R. 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28,3.31). $40.00 per property +					$
TOTAL FEES ENCLOSED =					$944.00
				Amount to be refunded	$
				charged	$

a. [ ] A check in the amount $_____ to cover the above fees is enclosed.

b. [X] Please charge my Deposit Account No. 14-1270 in the amount of $ 944.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fee, with the exception of the Basic Issue Fee, which may be required, or credit any overpayment to Deposit Account No. 14-1270. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 C.F.R. 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Corporate Patent Counsel
Philips Electronics North America Corporation
580 White Plains Road
Tarrytown, NY 10591

(SIGNATURE)

Michael E. Marion
(NAME)

32,266
(REGISTRATION NUMBER)

S:\PI\MP26PI\A0.RU0.doc

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of — Atty. Docket

BERNHARD FISCHER — PHD 99,207

Serial No. — Group Art Unit

Filed: CONCURRENTLY — Ex.

Title: AVOIDANCE OF POISONING EFFECTS DURING ANESTHESIA

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to calculation of the filing fee and examination, please amend the above-identified application as follows:

IN THE CLAIMS

Please amend the claims as follows:

3. (amended) The system (10) of claim 1, wherein the anesthetic agent degradation product is carbon monoxide CO.

3. (amended) The system (10) of claim 1, wherein the anesthetic agent degradation product is carbon monoxide CO.

4. (amended) The system (10) according to claim 1, wherein the anesthetic agent degradation product is trifluoromethane, CHF_3, preferably as an indicator for the presence of CO in the gas mixture.

REMARKS

The foregoing amendments to the claims were made solely to avoid filing the claims in the multiple dependent form so as to avoid the additional filing fee.

The claims were not amended in order to address issues of patentability and Applicant respectfully reserves all rights he may have under the Doctrine of Equivalents. Applicant furthermore reserves his right to reintroduce subject matter deleted herein at a later time during the prosecution of this application or continuing applications.

Respectfully submitted,

By
Michael E. Marion, Reg. 32,266
Attorney
914) 333-9641

APPENDIX

3. (amended) The system (10) of claim ~~1 or 2~~, wherein the anesthetic agent degradation product is carbon monoxide CO.

4. (amended) The system (10) according to ~~any one of the above claims~~claim 1, wherein the anesthetic agent degradation product is trifluoromethane, CHF_3, preferably as an indicator for the presence of CO in the gas mixture.

AVOIDANCE OF POISONING EFFECTS DURING ANESTHESIA

BACKGROUND OF THE INVENTION

The present invention relates to poisoning effects during anesthesia.

During anesthesia with one of the agents desflurane, isoflurane or enflurane, it has been observed that patients can accidentally become exposed to carbon monoxide, CO, thus leading to an inadvertent CO-poisoning of the patient. Peter B. Berry et al. in "*Severe Carbon Monoxide Poisoning during Desflurane Anesthesia*", Anesthesiology V 90, No. 2, Feb 1999, p. 613 report 36% COHb as highest CO level in blood due to this effect, i.e. 36% of hemoglobin loaded with CO (instead of oxygen) after only 15 min of anesthesia time with desflurane. A degradation of the anesthetic agent used in conjunction with Baralime or Sodalime, generally used as absorber material for CO_2 in circle breathing systems, has been identified as origin of this exposure. It has been found that degradation of the agent occurs under a condition that the CO_2 absorber material is too dry. Carbon monoxide, CO, has been identified as one of the degradation products.

Usually, the accidental CO exposure goes undetected, because CO is not identified or measured by the commercially available medical gas monitors. Although clinicians are aware of the potential problem, its early recognition and immediate remedy requires experience and a thorough knowledge of the behavior of the monitoring equipment used. In the above case, described by Peter B. Berry et al., the detection occurred through a sequence of strange observations, 1st the oxygen saturation of the patient decreased to 93% in spite of a fresh gas flow with 100% oxygen, 2nd the gas analyzer being set to automatic agent identification mode suddenly switched to „enflurane" in spite of the desflurane used. Only then, the

clinicians suspected CO poisoning resulting from desiccation of the CO_2 absorber. A blood analysis for COHb confirmed that suspicion.

The intoxication by CO occurs through the strong binding of this molecule to hemoglobin in competition to the binding of oxygen. The affinity of hemoglobin to CO, however, is 300 times stronger than to oxygen. Therefore, it is a question of the dosage of CO that determines the COHb level in blood. Harrison N. et al. in Anesthesia, Vol. 51, p 1037-1040 (1996) notes that a CO level of 0.1% for 1 h gives a COHb level of approximately 30% and evidence of moderate to severe toxicity. In the case reported by Peter B. Berry et al., the measured COHb level was 36% after 15 min of anesthesia time. It can be concluded that the CO concentration in the inhaled gas stream in his reported case must have been of the order of 0.5%.

Gas analyzers normally applied in anesthetic environments are based on gas detection by absorption measurements. Primarily, the infrared (IR) spectral region is used. The unusual behavior of the gas analyzer in the above reported case was explained by the similarity of the infrared absorption spectrum between another degradation product trifluoromethane, CHF_3, and enflurane, thus leading to the erroneous identification of the anesthetic agent.

It has been speculated by Harvey J. Woehlck in *"Severe Intraoperative CO Poisoning"*, Anesthesiology V 90, No. 2, Feb 1999, p. 353 (Editorial), that a very large number of patients are at risk to be exposed to undetected CO levels, in particular the first cases in the morning or cases on anesthesia machines that are infrequently used. Also, the use of a high flow of fresh (dry) gas enhances the likelihood that the CO_2 absorber material becomes desiccated and starts to break down the agent molecules.

The complete avoidance of the described problem would require strict discipline

with the renewal/exchange routine of the CO_2 absorber material (cf. Harvey J. Woehlck et al., Reduction in the Incidence of Carbon Monoxide Exposures in Humans Undergoing General Anesthesia, Anesthesiology V87, No 2, Aug 1997, p. 228). However, since this strict discipline with the renewal/exchange routine appears to be hardly feasible, an early and unambiguous identification of CO gas would be desirable. The gas monitors presently used in clinics, however, are not capable of detecting CO and react only indefinitely to its presence in the breathing gas mixture and mostly provide erroneous information to the user.

SUMMARY OF THE INVENTION

It is therefore an object of the invention to avoid poisoning effects during anesthesia. The object is solved by the independent claims. Preferred embodiments are shown by the dependent claims.

According to the invention, the CO concentration in a respiration gas is directly and/or indirectly measured in a substantially continuous monitoring process. An alarm will be provided when the monitored concentration exceeds one or more given threshold values. Thus, a timely warning can be issued so that the clinical personnel can replace the CO_2 absorber material before any harm will be done to the patient.

An indirect monitoring of the CO concentration in a respiration gas is applied by measuring a by-product of the anesthetic agent degradation process other than CO. Preferably, a by-product is selected which is absorbed in the body to a much lower degree than CO and thus easier to detect than CO. The by-product is thus employed as an indicator for the presence of CO. Preferably, trifluoromethane, CHF_3, is employed as such an indicator. CHF_3 can be detected using Raman or IR spectroscopy.

It has been shown that the physiologically relatively harmless CHF_3 provides an excellent indicator for the presence of the dangerous CO. Since CO is virtually "sucked" by the lungs into the blood, the CO concentration in the respiration circle normally remains relatively low. The concentration of CHF_3, in contrast thereto, will be accumulated in the respiration circle, because CHF_3 is normally bound or absorbed in the body to a much lower degree than CO. Therefore, the concentration of CHF_3 in the respiration circle will be normally much higher than the concentration of CO and is thus much easier to detect.

A direct monitoring of the CO concentration in a respiration gas is applied using Raman spectroscopy for directly detecting the presence of anesthetic agent degradation products in a respiration gas such as CO and/or any other degradation product, like CHF3, which can be employed as an indicator for the presence of CO.

The invention preferably applies **Raman scattering** for gas analyzing purposes. Gas detection, in general, is accomplished either by using optical absorption or by scattering of light. Scattering of light occurs as a consequence of the electronic polarizability of the electron cloud around atoms and molecules. Most incident photons are scattered by the sample with no change in frequency in a process known as Rayleigh scattering. Rayleigh scattering occurs from molecular as well as atomic species. However, with a small probability the scattered photons have frequencies $f_0 +/- f_1$, where f_0 is the frequency of the incident photon and f_1 is the frequency of a molecular vibration. This process is called Raman scattering. The modification of the scattered photons results from the incident photons either gaining energy from or losing energy to the vibrational or rotational motion of the molecule. Since complex molecules exist in a number of different rotational and vibrational states (depending on the temperature), many different values of f_1 are possible. Consequently, the Raman spectrum of a ***Raman-active gas*** will consist of a large number of scattered lines. Simple diatomic molecules like oxygen, O_2, or

nitrogen, N_2, have just one Raman line.

To enhance the observation of the radiation at f_0 +/- f_1, the scattered radiation is observed perpendicularly to the incident beam. To provide high intensity incident radiation and to enable the observation of lines where f_1 is small (due to rotational changes), the source of a Raman spectrometer is normally chosen as a monochromatic visible laser. The scattered radiation can then be analyzed by use of a scanning optical monochromator with a photomultiplier tube or another suitable photo detector.

Gas analyzers employing Raman spectroscopy can be calibrated to various Raman-active gases. The spectral „fingerprint" of Raman-active gases can be used to identify constituents of even very complex gas mixtures, and the relative intensity of the spectral contributions by each member gas is used to quantify the gases.

In a preferred embodiment of the invention, a gas analyzer employing Raman spectroscopy is calibrated to one or more anesthetic agent degradation products such as CHF_3, CO and/or other species of interest, normally in addition to the usual respiratory and anesthetic gases. Calibration herein means that a reference spectrum of the respective Raman-active gas is stored and will be used for detecting the respective Raman-active gas. As soon as the Raman gas monitor detects amounts of unwanted species exceeding pre-given threshold values, a warning sign will be generated thus alerting e.g. the clinician and giving direct and clear information about the origin and nature of the problem.

In one embodiment, a (direct) CO detection and monitoring is applied for generating a warning signal against impending CO poisoning. In another embodiment, the detection of any other degradation product like the CHF_3 compound is employed. CHF_3 gives a very strong Raman signal, and it has been verified that the lower

detection limit is well below 0.1%. CO is strongly bound to hemoglobin (the affinity of Hb to CO is 300 times larger than to oxygen) such that inhaled gas gets depleted from CO very effectively, while the CHF_3 stays in the breathing circuit and rapidly enriches to higher concentrations. Therefore, CHF_3 represents a fairly good indicator gas for CO presence.

In a preferred embodiment of the invention, a Raman gas analyzer is employed using a laser source in the visible spectral region to excite the Raman spectrum. The Raman gas analyzer might further be equipped with a spectrometer to measure Raman lines in a spectral range of preferably about 200 nm from the excitation wavelength. This gas analyzer can be calibrated for Raman-active gases by exposing the Raman measurement cell to a pure sample (or diluted mixture) containing this gas and recording the respective Raman spectrum as a calibration spectrum. This way, the analyzer can be calibrated for CO and/or CHF_3, also in addition to the other respiratory and anesthetic gases of interest to the user.

An alarming algorithm is implemented preferably triggered by the detection of CO and/or CHF_3 in the breathing gas stream during clinical use. This alarm indicates to a user to check the CO_2 absorber and to exchange it against fresh material immediately in order to avoid CO poisoning of the patient.

The gas monitor in accordance with the present invention provides an early warning capability against CO poisoning and permits that accidental CO poisoning by the described degradation process can be reliably avoided. Although there is great uncertainty in the medical literature about the true morbidity from interoperative CO poisoning and about the resulting economic damage, it is well known that even moderate levels of a few percentage of COHb in patients undergoing cardiac, cranial, or spinal surgery may cause severe oxygen deficiencies. Prolonged oxygen deficiency leads to neurological disorders.

A further possibility for determining anesthetic agent degradation products is to use infrared absorption spectroscopy for the detection of CO and/or CHF_3. However, the larger widths and overlaps in IR absorption bands of the species of interest render the identification task to be fairly complex. A currently available medical gas analyzer would have to be fitted with additional optical filters, and the algorithms would have to be changed accordingly. The effort for both is very costly.

BRIEF DESCRIPTION OF THE DRAWINGS

Other objects and many of the attendant advantages of the present invention will be readily appreciated and become better understood by reference to the following detailed description when considering in connection with the accompanied drawings. Features that are substantially or functionally equal or similar will be referred to with the same reference sign(s).

Fig. 1 depicts the schematic view of a gas monitor 10 according to the invention, and

Fig. 2 shows an example of a measurement of a composition of a gas mixture with a number of gas constituents.

DETAILED DESCRIPTION OF THE INVENTION

Fig. 1 depicts the schematic view of a gas monitor 10 according to the invention. A gas flow 20 with a gas mixture such as a respiration gas is directed through a sample cell 30. An incident light beam 40, e.g. from a laser source, is scattered in the sample cell 30 and a scattering light 50 is received by a spectrograph 60. The spectrograph 60 is further coupled to a processing unit 70 for determining the composition of the gas mixture in the gas flow 20.

The processing unit 70 is preferably further connected (not shown) to the source of

the light beam 40 for receiving information about the light beam 40, such as the intensity. The processing unit 70 is preferably further coupled to a (not shown) pressure determining means and a temperature sensor within the sample cell 30 for receiving information about the pressure and temperature therein.

In a first step, the spectrograph 60 of the gas monitor 10 measures the Raman spectrum of the gas mixture. In a second step, the processing unit 70 then determines the quantitative amount of one or more anesthetic agent degradation products in the gas mixture of the gas flow 20 by comparing the measured Raman spectrum with stored reference spectra of anesthetic agent degradation products. Each reference spectrum generally represents the Raman spectrum for the pure gas component, determined under known conditions, e.g. a known condition of pressure and/or temperature within the sample cell 30 and of the intensity of the incident light beam 40. Accordingly, reference spectra can be applied already representing a defined gas mixture. The proportion of the measured spectrum to each reference spectrum provides a direct measure of the proportion of the individual gas component (represented by the reference spectrum) in the gas mixture.

The assignment of the peak(s) in the measured spectrum to the individual gas component(s) can be done as known in the art, e.g. by comparing the wavelength(s) of the peak(s) with the wavelength(s) of the reference spectrum/spectra of the individual gas component(s).

The comparison of the measured Raman spectra with the reference Raman spectra is preferably accomplished by determining the ratio of the amplitudes (intensities) for each wavelength channel of the spectrograph. However, other comparison methods e.g. by means of the peak area or the like can be applied accordingly.

In case that a certain individual gas component reveals more than one Raman line, all lines are preferably attenuated substantially evenly, so that, for the purpose of the invention, it is normally sufficient to evaluate only one Raman line for each gas component for determining the proportion of the individual gas component in the gas mixture.

The reference spectra comprising the wavelength positions and intensities are preferably determined by previous measurements and can be stored e.g. in a calibration matrix.

In case that the actual measuring conditions deviate from the measuring conditions of the reference spectra, the measured spectra have to be corrected, e.g. for the effects of pressure, temperature, and light intensity changes, using well-known algorithms.

Fig. 2 shows an example of a measurement of a composition of a gas mixture with a number of gas constituents. The spectrograph 60 measures a Raman spectrum 100 of the gas mixture. The wavelength position and intensities of a plurality of Raman lines are stored in a calibration matrix 110 with a plurality of individual reference spectra 110A...110Z for several gas constituents.

The measured spectrum 100 of the gas mixture is compared with the respective reference spectra 110A, 110B of the calibration matrix 110. The proportions of the peak levels from the reference spectra 110A, 110B, and 110Z to the measured spectrum 100 provides a direct measure for the proportions of the individual components in the gas mixture. In the example of Fig. 2, the wavelength and characteristics of the measured peaks refer to N_2, O_2, CHF_3, and CO. In this example, the peak N_2 shall represents 77% of the reference peak for N_2 in the reference spectrum 110A, the peak O_2 represents 21% of the reference peak for O_2

in the reference spectrum 110B, and both CHF_3 peaks (to the very left and right in the spectrum 100) represents 1% of the reference peak for CHF_3 in the reference spectrum 110Z. The peak CO represents about 0.5% of the reference peak for CO (not shown in 110). Accordingly, the gas composition of the measured spectrum 100 is: 77% of N_2, 21% of O_2, 1% of CHF_3, and about 0.5% of CO.

When the determined quantitative amount of one or more of the anesthetic agent degradation products in the gas mixture exceeds given threshold values for each of the degradation products, an alarm will given in a third step. The determination of reasonable threshold values for the detection of the degradation products is of course dependent on the sensitivity of the specific embodiment of the measurement system. Since one dangerous aspect of CO poisoning is the dose (the dose being the concentration multiplied by the exposure time) deposited in the blood hemoglobin, the optimization of the threshold values should preferably take into account both the detection limits for the degradation products as well as the system's integration time associated with those detection limits. On one hand, it is desirable to have threshold values as low as possible in order to generate a warning as early as possible, but, on the other hand, false-positive alarms triggered in an overly sensitive system are to be avoided, too. In a preferred embodiment, threshold values of 0.5% for CHF_3 and/or 0.2% for CO have been proved satisfactory. If more than one degradation product are monitored simultaneously a further increase in reliability of the alarm can be obtained from correlating the detection of these products at concentrations above the set threshold values.

In another preferred embodiment, only one of the anesthetic agent degradation products is used for monitoring possible CO-poisoning of patients in anesthesia. Preferably, only CHF_3 will be monitored since CHF3 provides a sufficiently strong Raman signal and it has been verified that the lower detection limit is well below 0.1%.

CLAIMS:

1. A system (10) for avoiding poisoning effects during anesthesia, comprising:

determining means (60, 70) for determining the quantitative amount of an anesthetic agent degradation product in an anesthetic gas mixture, and

alarm means for providing an alarm when the determined quantitative amount of the anesthetic agent degradation product in the anesthetic gas mixture exceeds a given threshold.

2. The system (10) of claim 1, wherein the determining means (60, 70) comprises:

measuring means (60) for measuring a Raman spectrum of the gas mixture, and

a processing unit (70) for determining the quantitative amount of the anesthetic agent degradation product in the gas mixture by comparing the measured Raman spectrum with a reference spectrum of the anesthetic agent degradation product.

3. The system (10) of claim 1 or 2, wherein the anesthetic agent degradation product is carbon monoxide CO.

4. The system (10) according to any one of the above claims, wherein the anesthetic agent degradation product is trifluoromethane, CHF_3, preferably as an indicator for the presence of CO in the gas mixture.

5. A system (10) for avoiding CO poisoning effects during anesthesia caused by anesthetic agent degradation products in a gas mixture such as a respiration gas, comprising:

means (60) for measuring a Raman spectrum of the gas mixture,

a processing unit (70) for determining the quantitative amount of at least one of the anesthetic agent degradation products, preferably CHF_3 and/or CO, in the gas mixture by comparing the measured Raman spectrum with a reference spectrum of the at least one anesthetic agent degradation products, and

means for providing an alarm when the determined quantitative amount of the anesthetic agent degradation product in the gas mixture exceeds a given threshold.

6. A method for avoiding poisoning effects during anesthesia, comprising the steps of:

(a) determining the quantitative amount of an anesthetic agent degradation product, preferably carbon monoxide CO and/or trifluoromethane CHF_3, in an anesthetic gas mixture, and

(b) providing an alarm when the determined quantitative amount of the anesthetic agent degradation product in the anesthetic gas mixture exceeds a given threshold.

7. The method of claim 6, wherein the step (b) comprises the steps of:

(c) measuring a Raman spectrum of the gas mixture, and

(d) determining the quantitative amount of the anesthetic agent degradation product in the gas mixture by comparing the measured Raman spectrum with a reference spectrum of the anesthetic agent degradation product.

8. Use of a Raman spectrometer (60, 70) for determining the quantitative amount

of an anesthetic agent degradation product in a gas mixture.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number
WO 01/15762 A1

(51) International Patent Classification⁷: A61M 16/01, 16/10, G01N 21/65

(21) International Application Number: PCT/EP99/06348

(22) International Filing Date: 28 August 1999 (28.08.1999)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant *(for all designated States except US)*: **HEWLETT-PACKARD COMPANY** [US/US]; Corporate Offices, 3000 Hanover Street, Palo Alto, CA 94304 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **FISCHER, Bernhard** [DE/DE]; Trochtelfinger Weg 12, D-71229 Leonberg (DE).

(74) Agent: **BARTH, Daniel**; Hewlett-Packard GmbH, Europäische Patent- und Lizenzabt., Herrenberger Strasse 140, D-71034 Böblingen (DE).

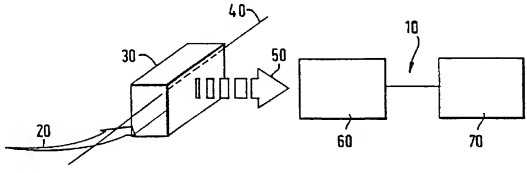
(81) Designated States *(national)*: JP, US.

(84) Designated States *(regional)*: European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AVOIDANCE OF POISONING EFFECTS DURING ANESTHESIA



(57) Abstract: For avoiding poisoning effects during anesthesia, the quantitative amount of an anesthetic agent degradation product, preferably carbon monoxide CO and/or trifluoromethane CHF_3, in an anesthetic gas mixture is determined. When the determined quantitative amount of the anesthetic agent degradation product in the anesthetic gas mixture exceeds a given threshold, an alarm is provided. This is preferably accomplished by measuring a Raman spectrum of the gas mixture, and determining the quantitative amount of the anesthetic agent degradation product in the gas mixture by comparing the measured Raman spectrum with a reference spectrum of the anesthetic agent degradation product.

WO 01/15762 A1

1 / 1

FIG. 1

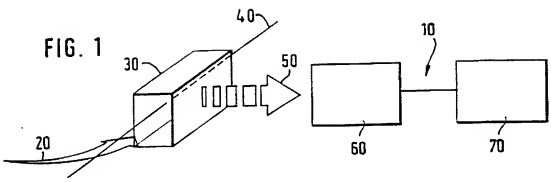
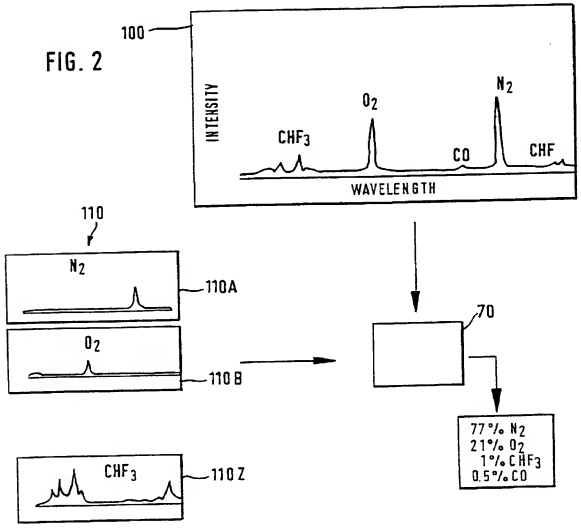

40
30
50
10
20
60
70

FIG. 2


100
INTENSITY
CHF_3
O_2
CO
N_2
CHF
WAVELENGTH
110
N_2
110A
O_2
110B
CHF_3
110Z
70
77% N_2
21% O_2
1% CHF_3
0.5% CO

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (includes Reference to PCT International Applications)	ATTORNEY'S DOCKET NUMBER **PHD 99.207 US**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **"Avoidance of poisoning effects during anesthesia"**,
the specification of which (check only one item below):

☐ is attached hereto.

☐ was filed as United States application

Serial No _____

on _____

and was amended

on _____

☒ was filed as PCT international application

Number PCT/EP99/06348

on 28 August 1999

and was amended under PCT Article 19

on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, § 1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR	PRIORITY CLAIMED UNDER 35 USC 119
WO	**PCT/EP99/06348**	**28 August 1999**	**YES**

Combined Declaration For Patent Application and Power of Attorney (Continued) (includes Reference to PCT International Applications)	Attorneys Docket Number **PHD 99.207 US**

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. (List name and registration number)

Jack E. Haken, Reg. No. 26,902 Michael E. Marion, Reg. 32,266 Edward M. Blocker, Reg. No. 30,245	Direct Telephone Calls to (name and telephone number) (914)332-0222

1-00	FULL NAME OF INVENTOR	FAMILY NAME **FISCHER**	FIRST GIVEN NAME **Bernhard**	SECOND GIVEN NAME
201	RESIDENCE & CITIZENSHIP	CITY **Leonberg** DEX	STATE OR FOREIGN COUNTRY **Germany**	COUNTRY OF CITIZENSHIP **Germany** ✓
	POST OFFICE ADDRESS	POST OFFICE ADDRESS **Trochtelfinger Weg 12**	CITY **Leonberg D-71229**	STATE & ZIP CODE/COUNTRY **Germany**

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true: and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 if Title 18 of the United states Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201
DATE

U.S. DEPARTMENT OF COMMERCE- Patent and Trademarks Office
(July 1994)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of — Atty. Docket

BERNHARD FISCHER — PHD 99,207

Serial No. — Group Art Unit

Filed: CONCURRENTLY — Ex.

Title: AVOIDANCE OF POISONING EFFECTS DURING ANESTHESIA

APPOINTMENT OF ASSOCIATES

Sir:

The undersigned Attorney of Record hereby revokes all prior appointments (if any) of Associate Attorney(s) or Agent(s) in the above-captioned case and appoints:

Tony Piotrowski **(Registration No. 42,080)**

c/o U.S. PHILIPS CORPORATION, Intellectual Property Department, 580 White Plains Road, Tarrytown, New York 10591, his Associate Attorney(s)/Agent(s) with all the usual powers to prosecute the above-identified application and any division or continuation thereof, to make alterations and amendments therein, and to transact all business in the Patent and Trademark Office connected therewith.

ALL CORRESPONDENCE CONCERNING THIS APPLICATION AND THE LETTERS PATENT WHEN GRANTED SHOULD BE ADDRESSED TO THE UNDERSIGNED ATTORNEY OF RECORD.

Respectfully,

Michael E. Marion, Reg. 32,266
Attorney of Record

Dated at Tarrytown, New York
this February 26, 2002

C:\jr\0forms\APPASOC.doc